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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,844	02/11/2004	Lon J. Wilson	1789-12301	3026

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EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
12/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pathou@conleyrose.com

Office Action Summary	Application No.	Applicant(s)	
	10/776,844	WILSON ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,23 and 27-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,23 and 27-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10,23 and 27-43 are pending in the application. Claims 11-18 were canceled and claims 36-43 were newly added in the amendment filed 11/18/08. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

New Grounds of Rejection Necessitated by the Amendment

Response to Arguments

Applicant's arguments with respect to claims 1-10,23 and 27-35 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-9,23,27-34 and 36-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolskar et al. (US2003/0220518A1) in view of Yan et al. (US 5,830,539) and in further view of Kelley et al. (US 6,958,216B2).

3. Bolskar et al. (US2003/0220518A1) discloses therapeutic and diagnostic fullerenes which are derivatized with at least two charged functional groups (and preferably more than two charged functional groups) to provide for water-solubility and improved in vivo distribution (abstract; p2, [0019]; p3, [0020], [0021] and [0024]; p11,

[0104]). The multiple functional groups that can be introduced onto the fullerene surface may be $-COOR_3$, $-P(O)(OR_3)_2$ (bone-targeting ligand), SO_2R_3, etc. and may be substituted directly on the fullerene ring or via a cyclopropane ring (p3, [0027]; p4, [0032] and [0034], p5, [0039]). Additionally the fullerene derivatives may be substituted with serinol groups, antibodies, peptides, fluorescent label, etc. (p6, [0045] and [0046]; claims 41 and 55). Bolskar et al. does not disclose that at least two antibiotic molecules are coupled to the fullerene molecule or that the targeting agents having at least one anthrax antigen bonding site, targeting agents derived from antibodies against anthrax, antibodies against anthrax spores, and combinations thereof.

4. Yan et al. (US 5,830,539) discloses coating/functionalizing substrates, such as fullerenes with a first layer comprising a molecular tether/linker covalently bonded to the surface and a second layer comprising therapeutic agents, diagnostic agents, antibodies, etc. bonded to the first layer (abstract; column 3, lines 9-12 and 42-47; column 4, lines 12-37). The functionalized fullerenes may be converted into devices having further functional groups attached to the first layer, such as targeting ligands (i.e. antigens), antibiotics, etc. (column 6, lines 45-49; column 7, lines 60-63).

5. Kelley et al. (US 6,958,216B2) discloses carbon nanotubes chemically attached to biomolecules wherein the biomolecules interact with target species that they are designed to "sense" and detect (abstract; column 2, lines 1-6). The biomolecule, 150 nucleotide fragment of the genome of *B. anthracis* was used for detecting DNA sequences of anthrax (column 14, lines 14-61 and 65).

6. At the time of the invention it would have been obvious and predictable to one ordinarily skilled in the art to derivatize the fullerenes of Bolskar et al. with antibiotics as taught by Yan et al. since the disclosures of Bolskar et al. and Yan et al. are both drawn to the derivatization of fullerenes. The attachment of the antibiotics of Yan et al. to the fullerenes of Bolskar et al. may obviously be via a cyclopropane ring containing the functional groups (i.e. $-COOR_3$, serinol, etc.) and thus would be coupled to the fullerene via a single linking molecule. It would also be obvious to one ordinarily skilled in the art to derivatize the fullerenes of the combined disclosures of Bolskar et al. and Yan et al. with targeting biomolecules that "sense" or detect anthrax as carbon nanotubes (Kelley et al.) are members of the fullerene structural family. The substitution of the targeting molecules/ligands of Kelley et al. for the targeting ligands of Bolskar et al. or Yan et al. is predictable as the disclosures are drawn to the functionalization of fullerenes (derivatives).

7. In regards to the antibiotic type, such as vancomycin, it is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect.

8. Claims 1-7,9,10,23,27-40,42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolskar et al. (US2003/0220518A1) and Yan et al. (US 5,830,539) and in view of Lei et al. (US 6,777,445B2).

9. Bolskar et al. (US2003/0220518A1) discloses therapeutic and diagnostic fullerenes which are derivatized with at least two charged functional groups (and preferably more than two charged functional groups) to provide for water-solubility and improved in vivo distribution (abstract; p2, [0019]; p3, [0020], [0021] and [0024]; p11, [0104]). The multiple functional groups that can be introduced onto the fullerene surface may be $-COOR_3$, $-P(O)(OR_3)_2$ (bone-targeting ligand), SO_2R_3, etc. and may be substituted directly on the fullerene ring or via a cyclopropane ring (p3, [0027]; p4, [0032] and [0034], p5, [0039]). Additionally the fullerene derivatives may be substituted with serinol groups, antibodies, peptides, fluorescent label, etc. (p6, [0045] and [0046]; claims 41 and 55). Bolskar et al. does not disclose that at least two antibiotic molecules are coupled to the fullerene molecule.

10. Yan et al. (US 5,830,539) discloses coating/functionalizing substrates, such as fullerenes with a first layer comprising a molecular tether/linker covalently bonded to the surface and a second layer comprising therapeutic agents, diagnostic agents, antibodies, etc. bonded to the first layer (abstract; column 3, lines 9-12 and 42-47; column 4, lines 12-37). The functionalized fullerenes may be converted into devices having further functional groups attached to the first layer, such as targeting ligands (i.e. antigens), antibiotics, etc. (column 6, lines 45-49; column 7, lines 60-63).

11. The combined disclosures of Bolskar et al. and Yan et al. do not disclose that fullerene-antibiotic conjugate comprises an aerosol mist or that the antibody is a TNF-alpha.

12. Lei et al. (US 6,777,445B2) discloses a water-soluble fullerene (C_{60}) derivative to treat bacterial or viral infections, such as *E. coli, Staphylococcus aureus*, etc. The use includes but is not limited to the related physiological conditions inhibiting cytokine, such as tumor necrosis factor-alpha (column 2, lines 7-14; column 3, lines 8-20; column 4, lines 10-20). Administration of a pharmaceutical formulation of the fullerene to a patient may include lubricating agents, carriers or may be made into aerosols (column 6, particularly line 48). The fullerene described contains multiple PO_3H, SO_3H, and CO_2H substituents that allow for bone-targeting bound to the fullerene molecules (column 5, lines 7-8).

13. At the time of the invention it would have been obvious and predictable to one ordinarily skilled in the art to derivatize the fullerenes of Bolskar et al. with antibiotics as taught by Yan et al. since the disclosures of Bolskar et al. and Yan et al. are drawn to the derivatization of fullerenes. The attachment of the antibiotics of Yan et al. to the fullerenes of Bolskar et al. may obviously be via a cyclopropane ring containing the functional groups (i.e. $-COOR_3$, serinol, etc.) and thus would be coupled to the fullerene via a single linking molecule. It would also be obvious to one ordinarily skilled in the art to derivatize fullerenes of the combined disclosures of Bolskar et al. and Yan et al. with targeting moieties that target tumor necrosis factor as the derivatized fullerenes of Lei et al. are taught to treat TNF-alpha and the fullerenes of Yan et al. and Bolskar et al. are taught to includes targeting ligands (i.e. antibodies).

14. In regards to the antibiotic type, such as vancomycin, it is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and

function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect.

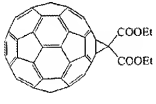
Response to Arguments

15. Applicant's arguments filed 11/18/08 have been fully considered but they are not persuasive.

16. In regards to newly added claims 36-43:

17. Claims 36-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolskar et al. (US 2003/0065206A1) in view of Yan et al. (US 5,830,539) and in further view of Kelley et al. (US 6,958,216B2).

18. Bolskar et al. (US 2003/0065206A1) discloses a derivatized fullerene comprising a malonate group (below) for water solubilization and for the incorporation of chemical handles for the attachment of other groups of biological interest (antibodies, proteins, peptides, ligands, drugs, etc.) (fig 1; p10, [0093]; p11, [0100]). Also, the fullerene of the disclosure may be derivatized with one or more chemical groups consisting of CR_1R_2 where R_1 and R_2 may be $P(O)(OH)_2$ (bone-targeting ligand).

19. 

20. Bolskar et al. does not disclose that the group of biological interest (drug) may be antibiotics or that the targeting agents having at least one anthrax antigen bonding site,

targeting agents derived from antibodies against anthrax, antibodies against anthrax spores, and combinations thereof.

21. Yan et al. (US 5,830,539) discloses coating/functionalizing substrates, such as fullerenes with a first layer comprising a molecular tether/linker covalently bonded to the surface and a second layer comprising therapeutic agents, diagnostic agents, antibodies, etc. bonded to the first layer (abstract; column 3, lines 9-12 and 42-47; column 4, lines 12-37). The functionalized fullerenes may be converted into devices having further functional groups attached to the first layer, such as targeting ligands (i.e. antigens), antibiotics, etc. (column 6, lines 45-49; column 7, lines 60-63).

22. Kelley et al. (US 6,958,216B2) discloses carbon nanotubes chemically attached to biomolecules wherein the biomolecules interact with target species that they are designed to "sense" and detect (abstract; column 2, lines 1-6). The biomolecule, 150 nucleotide fragment of the genome of *B. anthracis* was used for detecting DNA sequences of anthrax (column 14, lines 14-61 and 65).

23. At the time of the invention it would have been obvious and predictable to one ordinarily skilled in the art to derivatize the fullerenes of Bolskar et al. with antibiotics taught by Yan et al. since the disclosures of Bolskar et al. and Yan et al. are drawn to the derivatization of fullerenes with drugs, ligands, etc. The attachment of the antibiotics of Yan et al. to the fullerenes of Bolskar et al. may obviously be via a cyclopropane ring containing the functional groups (i.e. $-COOR_3$, etc.) and thus would be coupled to the fullerene via a single linking molecule. It would also be obvious to one ordinarily skilled in the art to derivatize the fullerenes of the combined disclosures of

Bolskar et al. and Yan et al. with targeting biomolecules that "sense" or detect anthrax as carbon nanotubes (Kelley et al.) are members of the fullerene structural family. The substitution of the targeting molecules/ligands of Kelley et al. for the targeting ligands of Bolskar et al. or Yan et al. is predictable as the disclosures are drawn to the functionalization of fullerenes (derivatives).

24. In regards to the antibiotic type, such as vancomycin, it is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect.

25. Applicant asserts that newly added claims recite specific antibiotic agents while Yan et al. broadly discloses the presence of antibacterial or antimicrobial agents.

26. Yan et al. teaches of fullerene molecules with a first layer comprising a molecular tether/linker covalently bonded to the surface and the attachment of antibiotics to this layer of fullerene molecules. Therefore it would have been obvious and predictable to one ordinarily skilled in the art to derivatize the fullerenes of Bolskar et al. with antibiotics taught by Yan et al. since the disclosures of Bolskar et al. and Yan et al. are drawn to the derivatization of fullerenes with drugs, ligands, etc. In regards to the antibiotic type, such as vancomycin, it is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect.

27. Applicant asserts that while Lei et al. teaches a mechanism of treating vancomycin-resistant organisms it is silent as to a fullerene-vancomycin conjugate.

28. The reference of Lei et al. was not used for the current rejection and therefore the assertion is moot.

Conclusion

29. No claims are allowed at this time.

30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618